



Dkt. 0575/69587-A-PCT-US/JPW/GJG/BJA/ML

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Nakanishi et al.
Serial No. : 10/579,162
International
Filing Date : November 9, 2004
For : SEPARATION OF GINKGOLIDE AND BILOBALIDE FROM G.
BILOBA

1185 Avenue of the Americas
New York, New York 10036
April 25, 2007

Mail Stop Amendment
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following items which are listed on the attached Form PTO-1449 (Exhibit A). Items 1-21 are U.S. Patents or U.S. Patent Application Publications. As permitted by 37 C.F.R. 1.98(a)(2)(ii), no copies of these items are included herewith. Copies of items 22-58 are attached hereto as Exhibits 1-37.

1. U.S. Patent No. 4,981,688, issued January 1, 1991, Ayroles et al.;
2. U.S. Patent No. 5,389,370, issued February 14, 1995, O'Reilly et al.;
3. U.S. Patent No. 5,399,348, issued March 21, 1995, Schwabe;

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4. U.S. Patent No. 5,466,829, issued November 14, 1995, Park et al.;
5. U.S. Patent No. 5,512,286, issued April 30, 1996, Schwabe;
6. U.S. Patent No. 5,599,950, issued February 4, 1997, Teng;
7. U.S. Patent No. 6,030,621, issued February 29, 2000, De Long et al.;
8. U.S. Patent No. 6,117,431, issued September 12, 2000, Ramazanov et al.;
9. U.S. Patent No. 6,143,725, issued November 7, 2000, Vasella et al.;
10. U.S. Patent No. 6,174,531, issued January 16, 2001, Zhang et al.;
11. U.S. Patent No. 6,187,314, issued February 13, 2001, Xie et al.;
12. U.S. Patent No. 6,221,356, issued April 24, 2001, Junsheng;
13. U.S. Patent No. 6,274,621, issued August 14, 2001, Drieu;
14. U.S. Patent No. 6,328,999, issued December 11, 2001, Schwabe;
15. U.S. Patent No. 6,590,109, issued July 8, 2003, Lichtblau et al.;

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16. U.S. Patent No. 6,884,451, issued January 18, 2005, Lichtblau et al.;
17. U.S. Patent No. 7,145,021, issued December 5, 2006, Stromgaard et al.;
18. U.S. Application Publication No. 2003-0194370, published October 16, 2003, Stromgaard et al.;
19. U.S. Application Publication No. 2003-0225052, published December 4, 2003, Stromgaard et al.;
20. U.S. Application Publication No. 2005-0119336, published June 2, 2005, Nakanishi et al.;
21. U.S. Application Publication No. 2005-0136136, published June 23, 2005, Lichtblau et al.;
22. U.S. Patent Application No. 11/634,429, filed on December 5, 2006, Stromgaard et al. **(Exhibit 1)**;
23. DE Patent No. 21 17 429 issued October 12, 1972 to Willmar Schwabe **(Exhibit 2)**;
24. UK Patent No. GB 2 288 599 A, issued November 25, 1995 to Cazaux et al. **(Exhibit 3)**;
25. PCT International Publication No. WO 93/02204, published February 4, 1993, on behalf of Han-Dok Remedial Ind. Co., Ltd. **(Exhibit 4)**;
26. PCT International Publication No. WO 99/52911, published

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on October 21, 1999 (Pietri et al.) **(Exhibit 5);**

27. PCT International Publication No. WO 02/083158, published on October 24, 2002, Societe De Conseils De Recherches et D'Applications Scientifiques **(Exhibit 6);**
28. PCT International Publication No. WO 03/082185 A1, published on October 9, 2003 (Kristian Stromgaard et al.) **(Exhibit 7);**
29. PCT International Publication No. WO 03/006040 A1, published January 23, 2003, Lichtblau et al. **(Exhibit 8);**
30. PCT International Publication No. WO 05/021496, published on March 10, 2005 (Koji Nakanishi et al.) **(Exhibit 9);**
31. PCT International Publication No. WO 05/046829, published on May 26, 2005 (Koji Nakanishi et al.) **(Exhibit 10);**
32. PCT International Publication No. WO 05/092324 (PCT/US05/009417), published on October 6, 2005 (Vitolo et al.) **(Exhibit 11);**
33. PCT International Publication No. WO 06/083366, published on August 10, 2006 (Koji Nakanishi et al.) **(Exhibit 12);**
34. PCT International Publication No. WO 07/002410, published on January 4, 2007 (Koji Nakanishi et al.) **(Exhibit 13);**
35. Ahlemeyer, B. et al., "Pharmacological Studies Supporting The Therapeutic Use of Ginkgo Biloba Extract For Alzheimer's Disease", PMID: 13130383 (2003) **(Exhibit 14);**

Applicants: Koji Nakanishi et al.

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36. Corey, E.J. & Su, W.G., "Total Synthesis of a C15 Ginkgolide, Bilobalide", J. Am. Chem. Soc., 1987, 109, 7534-7536 (**Exhibit 15**);
37. Corey, E.J. et al., "Total Synthesis of Ginkgolide Bilobalide", J. Am. Chem. Soc., 1988, 110, 649-651 (**Exhibit 16**);
38. Corey, E.J. & Ghosh, A.K., "Total Synthesis of Ginkgolide A", Tetrahedron Lett., 1988, 29, 3205-3206 (**Exhibit 17**);
39. Corey, E.J. & Gavai, A.V., "Simple Analogs of Ginkgolide B Which Are Highly Active Antagonists of Platelet Activating Factor", Tetrahedron Lett., 1989, 30, 6959-6962 (**Exhibit 18**);
40. Corey, E.J. et al., "Enantioselective Total Synthesis of Ginkgolide Derivatives Lacking the Tert-Butyl Group, an Essential Structural Subunit for Antagonism of Platelet Activating Factor", Tetrahedron Lett., 1991, 32, 4623-4626 (**Exhibit 19**);
41. Hu, L. et al., "Chemistry of Ginkgolides: Structure-Activity Relationship As PAF Antagonists", Pure Appl. Chem., 1999, 71, 1153-1156 (**Exhibit 20**);
42. Hu, L. et al., "Alkyl and Alkoxy carbonyl Derivatives of Ginkgolide B: Synthesis and Biological Evaluation of PAF Inhibitory Activity", Bioorg. Med. Chem., 2000, 8, 1515-1521 (**Exhibit 21**);

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43. Hu, L. et al., "New Products From Alkali Fusion of Ginkgolides A And B", J. Asian Nat. Prod. Res., 2000, 2, 103-110 **(Exhibit 22)**;
44. Hu, L. et al., "Synthesis And Biological Activity of Amide Derivatives of Ginkgolide A", J. Asian Nat. Prod. Res., 2001, 3, 219-227 **(Exhibit 23)**;
45. Jaracz et al.; "Ginkgolides: Selective Acetylations, Translactonization, and Biological Evaluation", J. Org. Chem., 2002, 67 (13): 4623-4626 **(Exhibit 24)**;
46. Lang, Q. et al. (2001) "Selective dissolution and one step separation of terpene trilactones in ginkgo leaf extracts for GC-FID determination," *Talanta* 54: 673-680 **(Exhibit 25)**;
47. McKenna, DJ et al., "Efficacy, safety, and use of ginkgo biloba in clinical and preclinical applications", PMID 11565403, 2003 **(Exhibit 26)**;
48. Supplementary European Search Report issued September 30, 2005 in connection with Application No. 02748132.4 **(Exhibit 27)**;
49. International Search Report issued 9/12/02 in connection with PCT/US02/22101 **(Exhibit 28)**;
50. International Search Report issued on 9/2/03 in connection with Application No. PCT/US03/12651 **(Exhibit 29)**;

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51. International Search Report issued 3/17/05 in connection with Application No. PCT/US04/27671 (**Exhibit 30**);
52. International Search Report issued 1/3/07 in connection with Application No. PCT/US06/24492 (**Exhibit 31**);
53. International Preliminary Examination Report issued 4/21/03 in connection with PCT/US02/22101 (**Exhibit 32**);
54. Tanaka, K. et al. (2005) "Unique Reactivity of α -Alkoxy Ginkgolide Lactones to Nucleophilic Reagents: Preparation of New Lactol Derivatives", Bull. Chem. Soc. Jpn., 78:1843-1850 (**Exhibit 33**);
55. Tanaka, K. et al. (2005) "Preparation of Ginkgolide and F-seco-ginkgolide Lactols: the Unique Reactivity of α -hydroxy Lactones toward NaBH₄", Tetrahedron Letters, 46:531-534 (**Exhibit 34**);
56. Vogensen, S.B. et al. (2003) "Preparation of 7-Substituted Ginkgolide Derivatives: Potent Platelet Activating Factor (PAF) Receptor Antagonists", J. Med. Chem., 46:601-608 (**Exhibit 35**);
57. International Search Report issued on 3/22/07 in connection with PCT/US05/42647 (**Exhibit 36**); and
58. Written Opinion of the International Searching Authority issued on 3/22/07 in connection with PCT/US05/42647 (**Exhibit 37**).

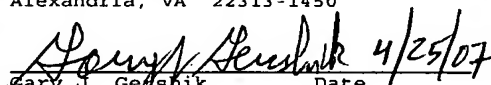
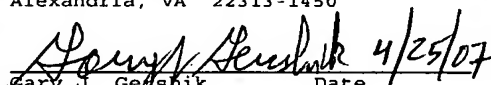
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This Supplemental Information Disclosure Statement is being submitted under 37 C.F.R. §1.97(b) and supplements the information disclosure statement filed by applicants on May 11, 2006 in connection with the above-identified application. Applicants request that the Examiner review the items listed and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	
 Gary J. Gershik Reg. No. 39,992	 Date 4/25/07

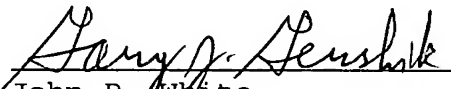

John P. White
Registration No. 28,678
Gary J. Gershik
Registration No. 39,992
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

EXHIBIT A



Form PTOL-1449

U.S. Department of Commerce
Patent and Trademark Office

Application Number	10/579,162
Filing Date	November 9, 2004
First Named Inventor	Koji Nakanashi et al.
Art Unit	
Examiner Name	
Attorney Docket No.	69587-A-PCT-US/JPW/GJG/BJA/ML

INFORMATION DISCLOSURE STATEMENT
(Use several sheets if necessary)

U.S. PATENT DOCUMENTS

Examiner Initials ¹	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		4,981,688	01-01-1991	Ayroles et al.
		5,389,370	02-14-1995	O'Reilly et al.
		5,399,348	03-21-1995	Schwabe
		5,466,829	11-14-1995	Park et al.
		5,512,286	04-30-1996	Schwabe
		5,599,950	02-04-1997	Teng
		6,030,621	02-29-2000	De Long et al.
		6,117,431	09-12-2000	Ramazanov et al.
		6,143,725	11-07-2000	Vasella et al.
		6,174,531	01-16-2001	Zhang et al.
		6,187,314	02-13-2001	Xie et al.
		6,221,356	04-24-2001	Junsheng
		6,274,621	08-14-2001	Drieu
		6,328,999	12-11-2001	Schwabe
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		2003-0194370	10-16-2003	Stromgaard et al.
		2003-0225052	12-04-2003	Stromgaard et al.
		2005-0119336	06-02-2005	Nakanashi et al.
		2005-0136136	06-23-2005	Lichtblau et al.
		11/634,429	12-05-2006	Stromgaard et al.

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Applicants: Koji Nakanashi et al.
Serial No.: 10/579,162
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Exhibit A

Form PTO-1449 U.S. Department of Commerce Patent and Trademark Office INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	Application Number	10/579,162
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	First Named Inventor	Koji Nakanashi et al.
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	Attorney Docket No.	69587-A-PCT-US/JPW/GJG/BJA/ML

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	T ⁶
		DE 21 17 429	10-12-1972	Schwabe	
		GB 2 228 599	11-25-1995	Cazaux et al.	
		WO 93/02204	02-04-1993	Han-Dok Remedia Ind. Co., Ltd.	
		WO 99/52911	10-21-1999	Pietri et al.	
		WO 02/083158	10-24-2002	Societe De Conseils De Recherches et D'Applications Scientifiques	
		WO 03/082185	10-09-2003	Stromgaard et al.	
		WO 03/006040	01-23-2003	Lichtblau et al.	
		WO 05/021496	03-10-2005	Nakanashi et al.	
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		WO 05/092324	10-06-2005	Vitolo et al.	
		WO 06/083366	08-10-2006	Nakanashi et al.	
		WO 07/002410	01-04-2007	Nakanashi et al.	

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Ahlemeyer, B. et al., "Pharmacological Studies Supporting The Therapeutic Use of Ginkgo Biloba Extract For Alzheimer's Disease", <u>PMID: 13130383</u> (2003)	
		Corey, E.J. & Su, W.G., "Total Synthesis of a C15 Ginkgolide, Bilobalide", <u>J. Am. Chem. Soc.</u> , 1987, <u>109</u> , 7534-7536	
		Corey, E.J. et al., "Total Synthesis of Ginkgolide Bilobalide", <u>J. Am. Chem. Soc.</u> , 1988, <u>110</u> , 649-651	
		Corey, E.J. & Ghosh, A.K., "Total Synthesis of Ginkgolide A", <u>Tetrahedron Lett.</u> , 1988, <u>29</u> , 3205-3206	

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		Corey, E.J. & Gavai, A.V., "Simple Analogs of Ginkgolide B Which Are Highly Active Antagonists of Platelet Activating Factor", <u>Tetrahedron Lett.</u> , 1989, <u>30</u> , 6959-6962			
		Corey, E.J. et al., "Enantioselective Total Synthesis of Ginkgolide Derivatives Lacking the Tert-Butyl Group, an Essential Structural Subunit for Antagonism of Platelet Activating Factor", <u>Tetrahedron Lett.</u> , 1991, <u>32</u> , 4623-4626			
		Hu, L. et al., "Chemistry of Ginkgolides: Structure-Activity Relationship As PAF Antagonists", <u>Pure Appl. Chem.</u> , 1999, <u>71</u> , 1153-1156			
		Hu, L. et al., "Alkyl and Alkoxycarbonyl Derivatives of Ginkgolide B: Synthesis and Biological Evaluation of PAF Inhibitory Activity", <u>Bioorg. Med. Chem.</u> , 2000, <u>8</u> , 1515-1521			
		Hu, L. et al., "New Products From Alkali Fusion of Ginkgolides A And B", <u>J. Asian Nat. Prod. Res.</u> , 2000, <u>2</u> , 103-110			
		Hu, L. et al., "Synthesis And Biological Activity of Amide Derivatives of Ginkgolide A", <u>J. Asian Nat. Prod. Res.</u> , 2001, <u>3</u> , 219-227			
		Jaracz et al.; "Ginkgolides: Selective Acetylations, Translactonization, and Biological Evaluation", <u>J. Org. Chem.</u> , 2002, <u>67</u> (13): 4623-4626			
		Lang, Q. et al. (2001) "Selective dissolution and one step separation of terpene trilactones in ginkgo leaf extracts for GC-FID determination," <u>Talanta</u> 54: 673-680			
		McKenna, DJ et al., "Efficacy, safety, and use of ginkgo biloba in clinical and preclinical applications", <u>PMID</u> 11565403, 2003			
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		Supplementary European Search Report issued September 30, 2005 in connection with Application No. 02748132.4	
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		Tanaka, K. et al. (2005) "Unique Reactivity of α -Alkoxy Ginkgolide Lactones to Nucleophilic Reagents: Preparation of New Lactol Derivatives", Bull. Chem. Soc. Jpn., 78:1843-1850	
		Tanaka, K. et al. (2005) "Preparation of Ginkgolide and F-seco-ginkgolide Lactols: the Unique Reactivity of α -hydroxy Lactones toward NaBH ₄ ", Tetrahedron Letters, 46:531-534	
		Vogensen, S.B. et al. (2003) "Preparation of 7-Substituted Ginkgolide Derivatives: Potent Platelet Activating Factor (PAF) Receptor Antagonists", J. Med. Chem., 46:601-608	
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